REMARKS

Claims 24-30, 32 and 34-38 are pending in the present application.

Rejection under 35 USC §102

Claims 24, 25 and 35-38 have been rejected under 35 U.S.C.§102(b) as being anticipated by Sugano et al. ('760). Applicants note that the Examiner previously rejected the now cancelled product claims in the Office Action of July 3, 2002 over the same reference of Sugano et al. ('760). Applicants demonstrated in the reply filed on January 3, 2003 that the method of making the extract as recited in claim 24 results in a product that is different from the product of Sugano et al. ('760). The Examiner is requested to reconsider the rejection in view of the remarks and evidence submitted in the January 3, 2003 response, wherein it was demonstrated that a product made using the recited method is different from the product of Sugano et al. ('760).

As discussed in the January 3, 2003 response, the method used to prepare the extract of used in the invention differs from the method used in Sugano et al. ('760). The present invention, as encompassed by claim 24, is drawn to a method using an extract of *Lentinus edodes* mycelium, which is prepared by

crushing and delignifying a solid medium containing *Lentinus edodes* mycelia in the presence of water and one or more enzymes selected from the group consisting of cellulase, protease and glucosidase, to prepare a suspension, wherein said solid medium is based on bagasse and defatted rice brand; and

raising the temperature of said suspension to inactivate the enzymes;

wherein said extract enhances γδT cell activity.

Thus, the invention of claim 24 is drawn to method that uses an extract product, which is defined, in part, by the process used to make it. The process used to make the extract used in the invention of claim 24 has three features.

i) the use of a solid bran medium based on bagasse and defatted rice bran;

ii) a step of crushing and delignifying a solid medium containing *Lentinus edodes* mycelia in the presence of water and one or more enzymes selected from the group consisting of cellulase, protease and glucosidase, to prepare a suspension; and

iii) a step of raising the temperature to inactivate the enzymes.

The method used to make the extract that is used in the method of the present invention results in a different product compared to Sugano ('760). For example, the product resulting from the extraction and preparation method of claim 24 has glucose as a primary component with a glucose content of approximately 40% (See Example 1 of the specification).

The extract of Sugano et al. ('760) "was found to contain sugar and protein primarily consisting of xylose" and the samples contained respectively 39.0% (LAP-1) and 30.4% (LAP-2) xylose. Thus, the resulting product used of the invention is different from the product of Sugano et al. ('760) due to the recited process of preparation. As such, the invention of claims 24, 25 and 35-38 is distinguished from Sugano et al. ('760) and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC §103

1) Claims 24-27, 30, 32, 34 and 35-38 have been rejected under 35 U.S.C.§103 as being obvious over Nagaoka (US '615) and Nagaoka (US '330) combined with Iizuka ('627). Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The rejection is based, in part, on the premise that the preparation of Iizuka ('627) is the same as the preparation used in the method of claim 24. (See page 5, of the Office Action.) Applicants similarly addressed the teachings of Iizuka ('627) in the reply filed on January 3, 2003. As noted in the response of January 3, 2003, Iizuka ('627) uses the same raw material and method of preparing an extract from *Lentinus edodes* as used in Sugano ('760). As such, the resulting extract from both references is the same. As noted previously, the preparation of both references lacks features i) and ii), above. Thus, the resulting product used in the invention is different from the product of Iizuka ('627) due to the recited process of preparation.

As such, the instant invention cannot be achieved by combining the reference teachings. Nor is there reasonable motivation to combine and modify Iizuka (US '627) with Nagaoka (US '615) and Nagaoka (US '330) to achieve the invention.

On page 6 of the current Office Action the Examiner addresses Applicants' arguments of December 13, 2006. The Examiner points to several sections of Nagaoka ('615) on page 7 of the Office Action as teaching the anti-tumor activity of the reference mycelium extract. However, all of the sections of Nagaoka ('615) that are relied upon by the Examiner refer to anti-tumor activity specifically in the context of β-glucan.

The instant claims recite that the enzyme is cellulase, protease and/or glucosidase. Column 6, lines 35-36 recite using cellulase, protease, β-1,3-glucanase and chitinase. Nagaoka ('615) further state that it is preferred that β-1,3-glucanase be present as the main component. See also the Abstract of Nagaoka ('615), which states that "Useful ingredients are extracted from a mycelium-containing culture medium by the steps of...separately, adding water and beta-1,3, glucanase and at least one enzyme selected from the group consisting of....." Thus, one skilled in the art would interpret Nagaoka ('615) as requiring digestion with β-1,3-glucanase. The purpose of using β-1,3-glucanase in Nagaoka ('615) is to obtain a product containing high levels of β-glucan. See the Abstract and column 4, lines 32-55. Nagaoka ('615) further teach that the β-glucan is the component responsible for the postulated, but not shown, antitumor activity as evidenced by the sections of the reference cited by the Examiner. Thus, one skilled in the art would conclude from the teachings of Nagaoka ('615) that β-glucan is an essential component for antitumor activity.

The presently claimed method uses a preparation digested with cellulase, protease and glucosidase, i.e. no β-1,3-glucanase. Concomitant with the absence of β-1,3-glucanase in the digestion of the preparation of the invention, the resultant composition of the method of claim 1 contains only negligible levels of β-glucan (0.0037%). Nagaoka ('615) teaches that β-glucan is the active component of the extract of the reference. One skilled in the art would not have any motivation to modify the reference teachings in a way that results in an extract that does not have the active component. In fact, one would be lead to conclude that such a modification would render the prior art extract ineffectual.

The instant invention, however, unlike Nagaoka ('615) does not rely on β-glucan for activity. β-glucan is believed to have anti-tumor effects through the activation of a humoral (i.e. B cell-mediated) immune response. The instant method on the other hand, is specifically limited to γδT cell activity, i.e. a specific T-cell population mediated immune response.

As such, one skilled in the art would not be motivated to modify Nagaoka ('615) by omitting digestion with β-1,3-glucanase and thereby having a composition that contains only negligible β-glucan. "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)" MPEP §2143.01. Modification of Nagaoka ('615) needed to achieve the invention, i.e. omission of digestion with β-1,3-glucanase, would render the extract of Nagaoka ('615) unsatisfactory for its intended purpose because such a modification would result in an extract having effectively no β-glucan, which Nagaoka ('615) teaches as being the active component.

In addition, as noted above combining Nagaoka ('615) with Iizuka ('627) would not achieve the invention because the extract of Iizuka ('627) is different than that used in the instant invention.

Regarding the alleged disclosure in Nagaoka ('330) for the anti-tumor activity, the reference contains even less relevant disclosure to the instant invention than Nagaoka '615. The sole disclosure Nagaoka ('330) regarding cancer is the recitation in claim 5 that the "viral disease" is liver cancer. Thus, Nagaoka ('330) is, in fact, not directed anti-tumor activity but rather anti-viral activity. As with the reasons discussed above regarding Nagaoka '615, there is no suggestion or disclosure in Nagaoka ('330) of treating a tumor with the specific extract recited in the claim, through the activation of γδT cell activity.

The indications in Nagaoka ('330) for treating viral diseases are apparent from the Title, the Abstract and the specification. See for example the "FIELD OF THE INVENTION" which states, "The present invention relates to an inhibitor of Hepatitis B virus and HIV (human immunodeficiency virus) activity." However, the disclosure in Nagaoka ('330) regarding the treatment of HIV or hepatitis B is not relevant to the instantly claimed invention of claim 26 and

dependent claims thereon, which require efficacy through the enhanced action of γδT cells. The Examiner specifically points to the disclosure at paragraphs [0013] and [0016] of the reference for disclosing the treatment of liver cancer. While the reference does not explicitly state that the liver cancer in question is of a viral cause, it is naturally flowing inference from the totality of the reference. The entire disclosure of Nagaoka ('330) pertains to the treatment of viral disorders as discussed above. It would be inconsistent and illogical for the inventors of Nagaoka ('330) to be referring to other than virally caused liver cancer in the paragraphs referred to by the Examiner. When reading the disclosure in Nagaoka ('330) one of ordinary skill in the art would conclude that the disclosure in paragraphs [0013] and [0016] is referring to the manifestation of a viral disease.

Nagaoka ('330) teaches that their extract of Lentinus edodes mycelium has an ability to enhance the activity of the T4 lymphocyte cell line, MT-4. As described in paragraph [0044] of Nagaoka '330, the MT-4 cell line was obtained by modifying human helper T cells with an adult T cell leukemia virus, i.e. MT-4 is an αβT cell. Thus, Nagaoka ('330) discloses the activation of αβT cells.

As noted, Nagaoka ('330) discloses the activation of αβT cells. However, αβ T cells are completely different from γδT cells with regard to characterization, function etc. One skilled in the art would not consider findings with αβT cells in any way predictive of or relevant to an activity of γδT cells. As such, there is no suggestion of the instant invention in Nagaoka ('330) and withdrawal of the rejection is respectfully requested.

In addition, as noted above combining Nagaoka ('330) with Iizuka ('627) would not achieve the invention because the extract of Iizuka ('627) is different than that used in the instant invention.

2) Claims 26-29 and 38 have been rejected under 35 U.S.C.§103 as being obvious over Nagaoka ('330) combined with Nagaoka ('816). Applicants traverse this rejection and withdrawal thereof is respectfully requested.

As noted previously, Nagaoka ('816) only discloses the **transdermal** antibacterial activity of an extract of *Lentinus edodes* mycelium. The present invention of claim 26 requires

administration orally or by injection. To find an invention obvious there must be some reasonable expectation of success. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 82 USPQ2d 1385 (U.S. 2007). The mechanism of action of the extract of the instant invention when administered orally or by injection is completely different from that of Nagaoka ('816). As such, there is no expectation of success from the cited references. Nor is there any motivation to modify the references so as to achieve the invention. As such, the instant invention is not obvious over Nagaoka ('330) combined with Nagaoka ('816).

3) Claims 24, 25 and 35-38 have been rejected under 35 U.S.C.§103 as being obvious over Sugano et al. ('760) combined with Nagaoka ('615). Applicants traverse this rejection and withdrawal thereof is respectfully requested. As discussed in detail above, the extract of Sugano ('760) is different from the extract used in the method of the instant invention. In addition, there is no motivation to modify the reference teachings so as to achieve the invention. As such, the instant invention cannot be achieved by combining Sugano ('760) with Nagaoka ('615).

Rejections for obviousness-type double patenting

Claims 24-30, 32 and 34-38 have been rejected for obviousness-type double patenting over claims 1-8 of US '081. Attached hereto is a terminal disclaimer filed in view of US '081. Withdrawal of the rejection is respectfully requested.

Possible restriction requirement

On page 14 that the Examiner "suggests" that the Applicant limit the claims to a single method to avoid a possible restriction requirement. Restriction at this point is improper. The Examiner has been searching and examining the various embodiments the invention for over 4 ½ years. Thus, it is clearly not been an undue burden. During that time Applicants have expended time and resources addressing various rejections made by the Examiner. To restrict the claims after 4 ½ years of examination would be highly prejudicial to Applicants and improper.

In view of the above Remarks, Applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D., Reg. No. 40,069 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By _____

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